UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,820	03/22/2001	Magnus Hook	P06357US02/BAS	8424

881 7590 12/13/2005

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,820	HOOK ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 12, 2005 has been entered. Claims 1 and 9 have been amended.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejection Withdrawn

3. Rejection of claims 1-16 under 35 U.S.C. 102(b), pages 3-4, paragraph 5 of the Final Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

4. Claims 1-16 are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8 are drawn to an isolated antibody that binds to the specific M31 subregion of a collagen binding domain having the sequence of amino acids 61-343 of the full length collagen binding protein of *Staphylococcus aureus* wherein said antibody prevents *S. aureus* infection.

Claims 9-12 are drawn to an isolated antibody that binds to the specific M31 subregion of a collagen binding domain having the sequence of amino acids 61-343 of the full length collagen binding protein of *Staphylococcus aureus* wherein said antibody treats *S. aureus* infection.

The claims are drawn to a vast genus of antibodies. To fulfill the written description requirements set forth under 35 USC,112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alliteratively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

To adequately describe the claimed genus of antibodies, Applicant must adequately describe the antigenic determinants (immunoepitopes) that elicit an immune response directed against *Staphylococcus aureus* not just those determinants that would elicit an immune response to the polypeptide since a given polypeptide can be immunogenic but not induce an directed immune response (i.e. immune response to *S. aureus*).

The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of antibodies to which the claims are drawn, such as a correlation between the structure of the immunoepitope and its recited function (to elicit an immune response directed against *S. aureus*), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of immunogenic compositions. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of immunoepitopes to which the claims are based. It should be noted that antibodies provide (at best) passive immunity and the specification fails to adequately describe any member of the claimed genus of antibodies capable of stimulating an immune response in an animal to *S. aureus* (either prophylactically or therapeutically).

MPEP 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention.* The invention is, for the purposes of the "written description" inquiry, *whatever is now claimed.*

See Vas-cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 17 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC j 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. M Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 US. C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, [p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a

representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed.

Enablement

5. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an isolated antibody that binds to the specific M31 subregion of a collagen binding domain having the sequence of amino acids 61-343 of the full length collagen binding protein of *Staphylococcus aureus* wherein said antibody prevents or treats *S. aureus* infection.

The specification teaches that the antibodies of the invention may be useful in treatment of *Staphylococcus aureus* infections (page 5). The instant specification teaches that antisera raised against and reactive with collagen binding protein (CBP) inhibits binding, promotes phagaocytosis and enhances intracellular killing by macrophages (page 19). Therefore, the specification contemplates that the

administration of antibodies reactive with CBP to at-risk subjects will be effective for prophylaxis of and in the case of infected subjects for therapy of bacterial infection (pages 19-20).

However, the fails to teach which, if any, antibodies are effective to prevent *S. aureus* infections. It should be noted that The term "prevents" encompasses the ability of the specific antigen to induce protective immunity to *Staphylococcus aureus* infection or disease induction. The specification fails to provide evidence that any of the claimed antibodies are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed antibodies for their intended purpose of preventing *S. aureus* infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The instant specification fails to demonstrate antibodies of the invention that bind to the M31 subregion of the collagen binding domain having the sequence of amino acids 61-343 of the full length collagen binding domain of *S. aureus* wherein the antibody treats or prevents infection cause by *S. aureus*. Example 6 of the instant specification discloses that when mice with sepsis was administered epitopes containing amino acids 61-343 of the full length CBP and challenged with *S. aureus* only 2 out of 14 mice survived. Moreover, the instant specification only discloses the administration of the "M31 subregion of the collagen binding domain having the sequence of amino acids 61-343 of the full length CBP (i.e. the protein administered)

but not a single example of administering the claimed antibody in order to protect against *S. aureus* infection (i.e. induce passive immunity). It should be noted that the claims are directed to antibodies that are capable of treating or protecting *S. aureus* infections and not just to bind the epitope itself.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Claims 1-8 recite the limitation "wherein said antibody prevents *S. aureus* infection". Hence, the instant claims encompass the ability of the claimed antibody to induce protective immunity to *Staphylococcus aureus infection* or disease induction. The prior art teaches that not all antibodies raised against S. aureus proteins are protective. This is evidenced by Nemeth et al *(Infection and Immunity 1995),* vol. 63, No. 2, p. 375-38) disclose that antibodies to capsular polysaccharides are not protective against *S. aureus* endocarditis (see the Abstract).

Claims 9-16 recite the limitation "wherein said antibody treat *S. aureus* infection". The instant specification does not teach a single working example that discloses administering the claimed antibody in order to treat against *S. aureus* infection. It should be noted that the claims are directed to antibodies that are capable of treating *S. aureus* infections and not just to bind the epitope itself.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to administering an antibody to a subject with a *S. aureus* infection would achieve a desire level of success of preventing *Staphylococcus* infection or disease, 3) there are no working examples which suggest that antibodies raised against the M31 subregion the collagen binding domain hiving sequence of amino acids 61-343 is successful in treating or protecting against *S. aureus* infections and 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level).

In view of all of the above, it is determined that the specification has not provided guidance that would enable one of skill in the art to be able to make and use the claimed invention commensurate with the claims. One of skill in the art would require undue experimentation to determine whether the claimed antibody can be used to treat or protect against S. *aureus* infection or diseases.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-16 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "...the specific M31 subregion...". It is unclear as to what Applicant is referring. What constitutes a non-specific M31 subregion with regard to the recited amino acid positions since not base sequence is claimed? Correction and/or clarification is requested.

7. Claims 1-16 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "...suitable for...". It is unclear as to what Applicant is referring. How is the antibody made suitable for various types of administration? Is the structure of the antibody changed to accommodate different modes of administration? Correction and/or clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1-16 are rejected under 35 U.S.C. 102(a) as anticipated by Patti et al *(The Journal of Biological Chemistry, 1995, Vol. 270, No. 20, p.. 12005-12011).*

Claims 1-16 are drawn to an isolated antibody that binds to the specific M31 subregion of a collagen binding domain having the sequence of amino acids 61-343 of the full length collagen binding protein of *Staphylococcus aureus* wherein said antibody prevents or treats *S. aureus* infection.

Patti et al teach polyclonal antibodies raised against the collagen adhesion of *S. aureus* (page 12005). Patti et al teach that the antibodies were raised against the M31 collagen binding segments since the antibodies were raised against amino acids 151-297 of the collagen binding domain (page 12006). Patti et al also teaches a monoclonal antibody raised against the collagen binding domain (page 12007). Claim limitations such as "wherein said antibody prevents *S. aureus* infection, "wherein said antibody prevents *S. aureus* infection in a human" and "wherein said antibody is suitable for parenteral, oral, intranasal, subcutaneous or intravenous administration to an animal" are being viewed as limitations of intended use. The claimed antibodies and the antibodies of the prior art would be necessarily the same since they were raised using

the same antigen, absence evidence to the contrary. Thus, the claimed antibodies and the antibodies of the prior art would have the same biological and immunological properties. The claim limitation "wherein the M31 subregion is encoded by a nucleic acid having the sequence of SEQ ID NO:3" would be inherent in teachings of the prior art since the claimed antibodies and the antibodies of the prior art were raised against the same antigen and hence they necessarily have the same sequence. Furthermore, discovery of a new property for a known product is not patentable. See MPEP 2112.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

9. No claims allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
December 8, 2005

ROBERT A. ZEMAN
PATENT EXAMINER